

Application No. 10/705,874

Please substitute the following claim set for the pending claim set.

1-89. (Cancelled)

90. (Currently amended) A method of karyotyping a genome of a test eukaryotic cell, comprising:

sequencing a population of identifying pieces of the genome of the test eukaryotic cell by determining to provide nucleotide sequence of said pieces;

matching, *in silico*, pieces of the genome to genomic locations using the nucleotide sequence of said pieces;

counting enumerating the pieces within a plurality of windows of a selected size throughout the genome to determine number of pieces as a function of genomic location fixed size of the genome, each of said windows having the fixed size, wherein each window comprises a plurality of pieces and the pieces within a window are genomically clustered pieces;

comparing the performing a plurality of comparisons for the plurality of windows in which a first number of pieces enumerated within a each window for the test eukaryotic cell is compared to the average number of pieces in windows of the selected size throughout the genome to obtain piece densities per window, wherein the piece densities per window represent the karyotype of the genome of a second number of pieces enumerated within the window for a reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

91. (Canceled)

92. (Currently amended) The method of claim 90 wherein the pieces within each of the windows ~~window~~ map within 40 kb.
93. (Currently amended) The method of claim 90 wherein the pieces within each of the windows ~~window~~ map within 200 kb.
94. (Currently amended) The method of claim 90 wherein the pieces within each of the windows ~~window~~ map within 600 kb.
95. (Currently amended) The method of claim 90 wherein the pieces within each of the windows ~~window~~ within 4 Mb.
96. (Previously Presented) The method of claim 90 wherein the pieces are defined by the presence of a Bcgl restriction endonuclease recognition site which is flanked by 12 nucleotides on either end.
97. (Currently amended) The method of claim ~~90~~ 113 further comprising the step of:
identifying aneuploidy if (a) pieces of one or more autosomes are determined to be present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (b) pieces of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (c) pieces of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.
98. (Currently amended) The method of claim 90 wherein pieces representing less than 15 % of the genome of the eukaryotic cell are ~~enumerated~~ sequenced, matched, and counted ~~in the step~~

~~of enumerating.~~

99. (Currently amended) A method of determining ~~changes~~ differences in copy number of portions of the genome of a test eukaryotic cell, comprising:

sequencing a population of ~~identifying~~ pieces of the genome of the test eukaryotic cell ~~by determining to provide~~ nucleotide sequence of said pieces;

matching, *in silico*, pieces of the genome to genomic locations using the nucleotide sequence of said pieces;

dynamically counting ~~enumerating~~ the pieces within a moving window of a selected size to determine number of pieces as a function of genomic location ~~plurality of windows of fixed size of the genome, each of said windows having the fixed size~~, wherein ~~each~~ the window comprises a plurality of ~~pieces and the pieces within a window are~~ genomically clustered pieces;

comparing the ~~performing a plurality of comparisons for the plurality of windows in which a first~~ number of pieces enumerated within ~~a~~ the window at a genomic location ~~for the test eukaryotic cell is compared to an average number of pieces in windows of the selected size throughout the genome to obtain piece density per window, a second number of pieces enumerated within the window for a reference eukaryotic cell, wherein a difference between the first number and the second number indicates a change in copy number of a portion of the genome between~~ in piece density per window between windows reflects a difference in copy number between portions of the genome ~~the test eukaryotic cell and the reference eukaryotic cell.~~

100. (Currently amended) The method of claim 99 wherein the ~~change~~ difference in copy number is due to gain or loss of a whole chromosome.
101. (Currently amended) The method of claim 99 wherein the ~~change~~ difference in copy number is due to a gain or loss of a chromosomal arm.
102. (Currently amended) The method of claim 99 wherein the ~~change~~ difference in copy number is due to an interstitial amplification.
103. (Currently amended) The method of claim 99 wherein the ~~change~~ difference in copy number is due to an interstitial deletion.
104. (Currently amended) The method of claim 99 wherein the pieces within ~~each~~ the window map within 40 kb.
105. (Currently amended) The method of claim 99 wherein the pieces within ~~each~~ the window map within 200 kb.
106. (Currently amended) The method of claim 99 wherein the pieces within ~~each~~ the window map within 600 kb.
107. (Currently amended) The method of claim 99 wherein the pieces within ~~each~~ the window map within 4 Mb.
108. (Previously Presented) The method of claim 99 wherein the pieces are defined by the presence of a Bcgl restriction endonuclease recognition site which is flanked by 12 nucleotides on either end.
109. (Currently amended) The method of claim ~~99~~ 113 further comprising the step of:
identifying aneuploidy if (a) pieces of one or more autosomes are determined to be present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or

greater or less than 0.7; or (b) pieces of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (c) pieces of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.

110. (Currently amended) The method of claim 99 wherein pieces representing less than 15 % of the genome of the eukaryotic cell are ~~enumerated~~ sequenced, matched, and dynamically counted ~~in the step of enumerating~~.

111. (New) The method of claim 90 or 99 wherein the sequencing is performed by automated nucleotide sequence determination.

112. (New) The method of claim 90 or 99 wherein between 100,000 and 1,000,000 pieces are sequenced and matched.

113. (New) The method of claim 90 or 99 further comprising the step of:
comparing piece densities per window for the test eukaryotic cell to piece densities of a reference eukaryotic cell.

114. (New) The method of claim 90 or 99 wherein the selected size is less than or equal to 40 kb.

115. (New) The method of claim 90 or 99 wherein the selected size is less than or equal to 200 kb.

116. (New) The method of claim 90 or 99 wherein the selected size is less than or equal to 600 kb.

117. (New) The method of claim 90 or 99 wherein the selected size is less than or equal to 4 Mb.